PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*)	08 JUN 2005
Applicant' s or agent's file reference 13627PCT	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/40034	29 November 2004 (29.11.2004)	28 November 2003 (28.11.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 38/17, 9/00; C07K 17/00 and US Cl.: 530/356, 355, 402, 418, 422, 427; 424/401, 423

Applicant

ALTERNATIVE SOURCED COLLAGEN, LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/40034

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/40034

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 2, 13, 15-20, 26, 30, 34 and 35	YES
	Claims 1, 3, 4-12, 14, 21-25, 27-29 and 31-33	NO
Inventive step (IS)	Claims None	YES
	Claims 1-35	NO
Industrial applicability (IA)	Claims 1-35	YES
	Claims None	NO

2. Citations and explanations:

Please See Continuation Sheet

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:
Claims 1, 3, 4, 6-12, 14, 21-25, 27 and 28 lack novelty under PCT Article 33(2) as being anticipated by Shadwick et al. Shadwick et al is directed like the instantly claimed invention to a collagen product derived from an animal, particularly marine animals such as from tuna tail tendons, the collagen product comprising precipitated collagen from acidic collagen dispersion, wherein the precipitated collagen is substantially pure collagen, wherein the precipitated collagen comprises two alpha 1(I) chains and one alpha 2(I) chain heterotrimer of collagen or type I collagen and is not derived from skin of an animal, and methods fro obtaining a collagen product thereof. The reference also teaches the distribution of amino acid composition of purified tendon collagen from tuna tail tendon which resembles the composition of Type I collagen found in tendons of other vertebrates and inherently the same with the claimed amino acid compositions of claims 4, 8 and 22. The reference also discloses that the collagen comprises 82% of the dry fraction, or 32% of the tissue wet weight which overlaps with the claims 0.01% to 100% by weight of collagen as claimed in claim 14. Thus, the prior art discloses the invention substantially as claimed, and as such, renders claims 1, 3, 4, 6-12, 14, 21-25, 27 and 28 as lacking novelty under PCT Article 33(2).

Claims 1, 5, 29 and 31-33 lack novelty under PCT Article 33(2) as being anticipated by Wolfinbarger, Jr. Wolfinbarger, Jr. is directed like the instantly claimed invention to a collagen fiber product derived from an animal, particularly from marine invertebrate Type V collagen, the collagen fiber product comprising adding an enzyme to collagen particles from the animal so as to substantially remove non-collagenous materials from the collagen particles, inactivating and washing the enzyme from the collagen particles, alkalinizing the collagen particles and neutralizing the alkalinized collagen particles with an acid to obtain a collagen dispersion, precipitating collagen fibers from the collagen dispersion to obtain the collagen fibers which are not derived from the skin of an animal. The reference also discloses cosmetic formulations containing a cosmetically effective amount of marine invertebrate Type V telopeptide collagen comprising 0.001 wt % to 30.00 wt % which overlaps with the claims 0.01% to 100% by weight of collagen as claimed in claim 14. Thus, the prior art discloses the invention substantially as claimed, and as such, renders claims 1, 5, 29 and 31-33 as lacking novelty under PCT Article 33(2).

Claims 1-35 lack an inventive step under PCT Article 33(3) as being obvious over Shadwick et al in view of Wolfinbarger, Jr., Nashihara and Shimizu et al. The primary reference of reference of Shadwick et al teaches the purification and characterization of a collagen product derived from an animal, particularly marine animals such as from tuna tail tendons, the collagen product comprising precipitated collagen from acidic collagen dispersion, wherein the precipitated collagen is substantially pure collagen, wherein the precipitated collagen comprises two alpha 1(I) chains and one alpha 2(I) chain heterotrimer of collagen or type I collagen and is not derived from skin of an animal, and methods fro obtaining a collagen product thereof. The reference also teaches the distribution of amino acid composition of purified tendon collagen from tuna tail tendon which resembles the composition of Type I collagen found in tendons of other vertebrates and expected to have the same properties with the claimed amino acid compositions of claims 4, 8 and 22. The reference also discloses that the collagen comprises 82% of the dry fraction, or 32% of the tissue wet weight which overlaps with the claims 0.01% to 100% by weight of collagen as claimed in claim 14.
The primary reference of Shadwick et al differs from claims 1-35 in not teaching a) the addition of an enzyme to remove non-collagenous materials, gelatin formation and cosmetic composition, b) use of deodorizing agent, c) a collagen product having 98 to

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

about 99% pure collagen, and d) crosslinking the collagen by thermal dehydration, chemical treatment, and/or light. However, the secondary reference of Wilfinbarger, Jr. teaches the production of a collagen fiber product derived from an animal, particularly from marine invertebrate Type V collagen, the collagen fiber product comprising adding an enzyme to collagen particles from the animal so as to substantially remove non-collagenous materials from the collagen particles, inactivating and washing the enzyme from the collagen particles, alkalinizing the collagen particles and neutralizing the alkalinized collagen particles with an acid to obtain a collagen dispersion, precipitating collagen fibers from the collagen dispersion to obtain the collagen fibers which are not derived from the skin of an animal. The reference also discloses the preparation of collagen gel, collagen gelatin and cosmetic formulations. Further, Nishihara teaches the preparation of shark-derived collagen by extracting the collagen with acid and desalted to obtain a liquid collagen. The resultant insoluble collagen is suspended in a buffer and desalted by a combination of, for example heating treatment and enzyme digestion to thereby obtain a liquid collagen containing a cosmetically effective amount of marine invertebrate Type V telopeptide collagen, wherein the concentration of the collagen solution is about 1 to 5% (w/v). Furthermore, the reference of Shimizu et al teaches the extraction and purification of fish skin collagen involving deodorization. For further support of subjecting to deodorization treatment and crosslinking the collagen by thermal dehydration under a vacuum at a temperature between 60 degree to about 130 degree Celsius, See U.S. Patent 6,660,280 which is applied as Y,P (document published prior to international filing date but later than the priority claimed) because such combination is obvious to a person skilled in the art as stated by the above cited reference. The reference also discloses that the collagen compound is a collagen hydrolysate.

With respect to the purity of collagen from 98% to about 99%, none of the cited prior art discloses such specific purity. However, each of the prior art of record teaches the extraction and purification of collagen derived from marine animals which are substantially pure. Thus, the difference appears to be in degree of purification and not in kind, and as such, it is within the purview of ordinary skill in the art to purify the specific degree of purity required (i.e., 98 to 99% purity) because the materials (i.e., marine collagen) intended to be purified is the same materials disclosed by the prior art which are substantially pure. Hence, the claims with regard to degrees of purity of the instant application is seen to be optimization of art recognized methods, and is seen to be within the purview of skilled artisan.

Therefore, in view of the above, and in view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated at the time the invention was made to use the already known collagen product derived from an animal, particularly marine animals, the collagen product comprising precipitated collagen from an acidic collagen dispersion, wherein the precipitated collagen is substantially pure or from about 98% to about 99% pure, wherein the precipitated collagen comprises two alpha1(i) chains and one alpha 2(I) chain heterotrimer of collagen or Type I collagen and is not derived from skin of an animal, and methods for obtaining collagen product or collagen fibers or gelatins thereof. Thus, the teachings of the prior art renders obvious the instant invention as claimed in claims 1-35.

Claims 2, 13, 15-20, 26, 30, 34 and 35 meet the criteria as set forth by PCT Article 33(2).
Claims 1-35 meet the criteria as set forth by PCT Article 33(4).